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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,208	07/20/2001	Jiro Hitomi	MM4454	4894

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
10/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/910,208	HITOMI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2010*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22 and 24-27* is/are pending in the application.

4a) Of the above claim(s) *24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 09/14/2010 and 09/22/2010, is acknowledged.

2. Claims 22 and 24-27 are pending.

3. Claims 24-27 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claim 22 is under consideration in the instant application as it reads on an antibody with binding affinity to a protein encoded by SEQ ID NO: 1.

5. In view of the amendment filed on 09/14/2010 and 09/22/2010, only the following rejections are remained.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 22 stands rejected under 35 U.S.C. 102(b) as being anticipated by Kelly *et al* (J. Patho. 1989) as is evidenced by Guignard et al (Feb 1996).

Kelly et al teach monoclonal antibodies to study the expression of calgranulins by keratinocytes in inflammatory dermatoses. Kelly et al also teach that calgranulins are intracellular calcium binding proteins which have inflammatory cytokine activity. Further, Kelly et al teach that MAC 387 monoclonal antibody that recognizes a molecule probable containing both calgranulin A and B (see abstract in particular). MAC 387 monoclonal antibody also binds amino acid sequence encoded by SEQ ID NO: 19, as is evidenced by Guignard et al (Feb 1996) that the immunoreactivity of MAC 387 was compared with that of a polyclonal antibody raised against purified MRP-8, but cross-reacting with MRP-14, and p6 (hCAAF1/S100A12), a novel S100 protein. Under such conditions, Mac 387 was found to recognize the three S100 proteins (see abstract in particular). Guignard et al concluded that the MAC 387 might recognize an epitope common to the proteins of the S100 family (see abstract last sentence). Guignard et al teach that all the S100 proteins have amino acid sequence and secondary-structure similarities in very specific and conserved regions which are the N- and C-terminal hydrophobic amino acid domains. They are also characterized by the presence of two calcium-binding sites called EF-hand, that contain 14 and 12 amino acids. Interestingly, the 14 amino acid EF-hand is conserved in all S100 proteins and is located in a conserved basic domain near the N-terminal part of the protein while the 12 amino acid EF-hand is located in a conserved acidic domain in the C-terminal region. These similarities make the generation of specific antisera difficult due to structural conservation and might explain the cross-reactivity of Mac 387 with MRP-14, MRP-8 and P6. If this mAb recognizes an epitope common to the proteins of S100 family, its use might allow the diction of novel members of this family (see page 106, under Discussion). Given that

the human an bovine CAAF1 share 66% sequence homology, the reference MAC 387 would bind the claimed bovine sequence of SEQ ID NO:19, in the absence of evidence to the contrary.

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibody does not bind to the SEQ ID NO:19 recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 09/14/2010, have been fully considered, but have not been found convincing.

Applicants submit that they have amended claim 22 into a "product-by-process" claim which, for purposes of examination, is a product claim in Group IV and not an assay method for a calcium binding protein in Group V. However, claim 22, as now amended, is directed to a diagnostic agent for diagnosing inflammatory diseases in Group IV but is otherwise limited to the process consistin.q of forming a calcium binding protein assay reagent composed of a monoclonal antibody specific to a calcium-binding protein comprising an amino acid sequence shown in SEQ ID NO:19 or encoded by a nucleic acid sequence shown in SEQ ID NO:I and using said calcium-binding protein assay reagent as the diagnostic agent to diagnose the presence of such diseases. Applicants contend that there is no teaching in Kelley of using a process consisting of forming a calcium-binding protein assay reagent composed of a monoclonal antibody as defined in claim 22 and using such calcium-binding protein assay reagent as the diagnostic agent to diagnose the presence of such diseases as called for in claim.

However, while the claim is constructed as product by process, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985), MPEP 2113. It is Applicant burden to show that the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.

Applicant submits that the Kelly reference carried out tissue staining of skin having inflammation using CF145 monoclonal antibody specific to calgranulin A, CF557 monoclonal antibody specific to calgranulin B, and MAC387 monoclonal antibody reactive both to calgranulin A and calgranulin B, and verified that calgranulin A and calgranulin B are stained in the skin tissue inflammation. However, they are not stained in skin tissue not having inflammation.

With respect to the issue that Kelly et al do not teach a diagnostic agent for inflammatory diseases, the Examiner notes that the claim recites the same products and the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the monoclonal antibody and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of

the claimed diagnostic agent. Regardless, the monoclonal antibody agent of the Kelly et al. reference is not incompatible with a diagnostic intention.

Applicant submits that CAAF1 of the present invention does not have high homology with calgranulin A or calgranulin B, though it has a high homology with calgranulin C. In addition, according to the Kelly reference on page 18, MATERIALS AND METHODS, Control experiment, although bands of 10.5kd and 13.5kD correspond to calgranulin A and calgranulin B were detected in Western blot experiment using an extract of skin tissue having inflammation, a band of 6kD corresponding to calgranulin C was not detected. Applicant concluded that the Kelly reference does not prove or suggest the existence of CAAF1 of the present invention nor is there any proof that calgranulin C was expressed in skin tissue. Moreover, it cannot be predicted from the teaching in the Kelly reference that CAAF1 of SEQ ID NO:19 will function as an inflammatory marker.

However, the arguments of counsel cannot take the place of objective evidence in the record. *In re Schulze*, 145 USPQ 716, 718 (CCPA 1965). The Examiner points to the Guignard et al (Feb 1996) teachings that the immunoreactivity of MAC 387 was compared with that of a polyclonal antibody raised against purified MRP-8, but cross-reacting with MRP-14, and p6 (hCAAF1/S100A12), a novel S100 protein. Under such conditions, Mac 387 was found to recognize the three S100 proteins (see abstract in particular). Guignard et al concluded that the MAC 387 might recognize an epitope common to the proteins of the S100 family (see abstract last sentence). Guignard et al teach that all the S100 proteins have amino acid sequence and secondary-structure similarities in very specific and conserved regions which are the N- and C-terminal hydrophobic amino acid domains. They are also characterized by the presence of two calcium-binding sites called EF-hand, that contain 14 and 12 amino acids. Interestingly, the 14 amino acid EF-hand is conserved in all S100 proteins and is located in a conserved basic domain near the N-terminal part of the protein while the 12 amino acid EF-hand is located in a conserved acidic domain in the C-terminal region. These similarities make the generation of specific antisera difficult due to structural conservation and might explain the cross-reactivity of Mac 387 with MRP-14, MRP-8 and P6. If this mAb recognizes an epitope common to the proteins of S100 family, its use might allow the diction of novel members of this family (see page 106, under Discussion). Given that the human an bovine CAAF1 share 66% sequence homology, the reference MAC 387 would bind the claimed bovine sequence of SEQ ID NO:19, in the absence of evidence to the contrary.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 22 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Dell'Angelica (JBC, 269(46): 28929-28936, 1994) as evidenced by the specification disclosure on page 40, lines 6-9, Bost et al. (Immunol. Invest. 1988; 17:577-586), in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1) OR U.S. Pat. No. 5,654,403 for the same reasons set forth in the previous Office Action mailed 06/10/2010.

Applicant's arguments, filed 09/14/2010, have been fully considered, but have not been found convincing.

Applicant submits that the Kelly reference carried out tissue staining of skin having inflammation using CF145 monoclonal antibody specific to calgranulin A, CF557 monoclonal antibody specific to calgranulin B, and MAC387 monoclonal antibody reactive both to calgranulin A and calgranulin B, and verified that calgranulin A and calgranulin B are stained in the skin tissue inflammation. However, they are not stained in skin tissue not having inflammation.

However, the 103 rejection was not made over Kelly reference. Moreover, the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the monoclonal antibody and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of the claimed diagnostic agent. Regardless, the monoclonal antibody agent produced by the combined reference teachings is not incompatible with a diagnostic intention.

Applicant submits that CAAF1 of the present invention does not have high homology with calgranulin A or calgranulin B, though it has a high homology with calgranulin C. In addition, according to the Kelly reference on page 18, MATERIALS AND METHODS, Control experiment, although bands of 10.5kd and 13.5kD correspond to calgranulin A and calgranulin B were detected in Western blot experiment using an extract of skin tissue having inflammation, a band of 6kD corresponding to calgranulin C was not detected. Applicant concluded that the Kelly reference does not prove or suggest the existence of CAAF1 of the present invention nor is there any proof that calgranulin C was expressed in skin tissue. Moreover, it cannot be predicted

from the teaching in the Kelly reference that CAAF1 of SEQ ID NO:19 will function as an inflammatory marker.

However, the 103 rejection was not made over Kelly reference.

Applicant argues that the Examiner alleges that according to the Dell 'Angelica reference, peptides T3 and T4 of calgranulin have 100% sequence homology with CAAF1 and based upon this, the Examiner further alleges that it should be easy to obtain an antibody specific to CAAF1. Even if it were possible to obtain, from the peptide teaching in Dell'Angelica, an antibody reactive with CAAF1, this does not prove or suggest that CAAF1 is a diagnostic agent or that it can be used as a diagnostic marker for diagnosing inflammations, cancers, dermatitis and blood diseases as specified in claim 22.

However, the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the monoclonal antibody and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of the claimed diagnostic agent. Regardless, the monoclonal antibody agent result from the combined reference teachings is not incompatible with a diagnostic intention claimed.

Applicant argues that claim 22 as now amended is limited to a diagnostic agent formed in accordance with a process consisting of forming a calcium binding protein assay reagent composed of a monoclonal antibody specific to a calcium-binding protein comprising an amino acid sequence shown in SEQ ID NO:19 or encoded by nucleic acid sequence shown in SEQ ID NO:I. This is clearly not suggested nor taught in Kelly or in Dell' Angelica for the reasons given above. Moreover, forming a calcium binding protein assay reagent as claimed does not suggest use of such calcium- binding protein assay reagent to diagnose the presence of the diseases specified in claim 22.

However, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985), MPEP 2113. It is Applicant burden to show that the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.

Applicant submits that the Examiner relative to a comparison of S100-1ike calcium-binding protein sequences which have sequence identities close to that of SEQ ID NO:19 is not applicable to clam 22 as currently amended since it is limited to a specific process consisting of a specific calcium binding protein assay reagent and not to other S100-1ike calcium-binding proteins and is also limited to a specific use which is clearly not taught or suggested in any of the references.

However, Applicant's argument attempts to limit the term "specific to a calcium-bin ding protein comprising an amino acid sequence shown in SEQ ID NO: 19" in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That is an antibody "cross-reacts", i.e., binds to more than one protein sequence, does not mean that the antibody does not "specifically bind" with both proteins. In the antibody art, cross-reactivity of prior disclosed antibodies with SEQ ID NO: 19 and the protein encoded by SEQ ID NO: 1 read on the claimed invention.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 7, 2010

/Maher M. Haddad/
Primary Examiner
Technology Center 1600